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## AN OVERVIEW OF NUTRACEUTICALS: CURRENT SCENARIO

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**ABSTRACT:** *Using food products to promote health and cure disease is renowned. Currently, most of the drug molecules available in the formulations were anciently used in their crude form. Dr Stephen De Felice first coins the term nutraceuticals in 1989 to provide medical or health benefits including the prevention and treatment of diseases. This review classified the large number of nutraceuticals available from various sources and its significance. Further, the regulatory status of nutraceuticals and latest trends in nutrigenomics are discussed.*

### KEY WORDS:

Nutraceutical, Dietary supplements, disease

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## INTRODUCTION

Since ancient period the mankind made medicines from the extracts of natural materials and has been used for various purposes. In 1989 Dr. Stephen coined the term "Nutraceuticals" which is combination of nutrition and pharmaceutical. Nutraceuticals have come a long way since a new trend in the care of companion animals emerged in the 1990s and the similar trends in the human sector as well. With the passage of the dietary supplement health and education act of 1994, the definition of nutraceuticals has been expanded to include vitamins, minerals, herbs and other botanicals, amino acids, and dietary substance for human use as a supplement diet <sup>(1)</sup>. The term nutraceutical is not well accepted on global, regulatory systems while the dietary supplements are considered to be more prominent. Currently over 470 nutraceutical and functional food products are available with documented health benefits <sup>(2)</sup>.

The success of traditional therapies is essentially due to the art of balancing the effect of one variety of food with other so that all complemented each

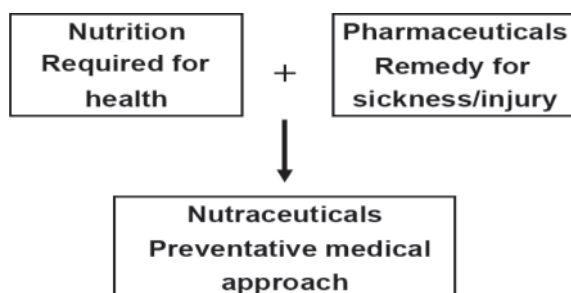
other. Currently, the medical practitioners are considered as magic wand to cure disease. A recent study reports that 70% of patients typically consult a medical practitioner before or during the traditional therapy, indicates the disapproval of the natural therapy <sup>(3)</sup>. However, the patients are much aware of the side effects, contraindications caused due to the chemical agents in short and long term therapy. Thus the interest to prevent medicine from every small disease came into trend and consequently led to new research on alternative therapies preferably with the help of nutritional approaches. This review gives highlights of some important facts regarding therapeutic use of nutraceuticals as the commercial and traditional remedies.

## CONCEPTS OF NUTRACEUTICALS

In the pharmaceutical development process, it is a requirement to have clinical test results from animal tests and studies, for verification of the effects. On the other hand, in the case of nutrition, there was no verification method for foods in preventing diseases in the past. In recent years however, as food composition has been scientifically proven to cause lifestyle-related diseases, and has become a social issue as figure 1.

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**Figure 1: Concept of Nutraceuticals**<sup>4</sup>

### REGULATORY ASPECTS OF NUTRACEUTICALS

The regulatory framework of nutraceuticals in India needs attention from the relevant authorities. Globally, the regulatory authorities are aware of changing needs of consumers and proactively protect consumers by amending existing laws to accommodate changes but in India old laws such as Prevention of Food adulteration Act, 1954, which regulates packaged foods, still exist for manufacturers. In addition, they need to abide by many other cumbersome laws such as:

- ✦ Standards of Weights and Measures Act, 1976, and the Standards of Weights and Measures
- ✦ (Packaged Commodities) Rules, 1977 (SWMA)
- ✦ Infant Milk Substitutes, Feeding bottles and infant foods (regulation of production, Supply and Distribution) Act, 1992 with Rules, 1993 (IMS)
- ✦ Edible Oils Packaging (Regulations) Order, 1998
- ✦ Fruit Products Order 1955 (FPO)
- ✦ Meat product Order 1973
- ✦ Milk and Milk Products Order 1992
- ✦ Vegetable Oils Products (Regulation) Order 1998 (VOP)
- ✦ Atomic Energy Act, 1962 and Atomic Energy (Control or irradiation of Food) Rules 1996
- ✦ Consumer Protection Act 1986 and the Consumer Protection (Amendment) Act, 2002 and Rules 1987
- ✦ Environment Protection Act, 1986 and Rules 1986
- ✦ Agricultural Produce (Grading and Marking) Act, 1937 (as amended up to 1986) and 49

- ✦ General Grading and Marking Rules 1986 and 1988 (AG Mark)
- ✦ Bureau of Indian Standards (BIS) Act 1986

Further, there is lack of clarity in classifying functional foods and Nutraceuticals. This causes confusion amongst the regulators. At times, the drug regulators are tempted to classify these products as drugs. This has resulted in trouble for genuine manufacturers. The revolutionary step to introduce Food Safety and Standards Act will replace the old PFA. The new act will take India on the path of new regulatory framework to make it capable of global competition<sup>(5)</sup>.

On the other hand in United States the Watershed legislation was passed in 1994 to regulate the manufacture and marketing of nutraceuticals. This law, known as the Dietary Supplement Health and Education Act (DSHEA), reversed 45 years of increasing FDA regulation of health-related products<sup>(6)</sup>. The passage of the Food and Drug Administration Modernization Act of 1997 (FDAMA) made additional options available to the manufacturers of nutraceuticals. This legislation was the result of a reform effort that spanned nearly two decades. It brings about a balance in FDA regulations between approving therapeutic products so that they can benefit patients and protecting public health by assuring that those products are safe and effective<sup>(7)</sup>. In 1993, the Ministry of Health and Welfare in Japan established a policy of "Foods for Specified Health Uses" (FOSHU) by which health claims of some selected functional foods are legally permitted. In 2001, a new regulatory system, foods with health claims (FHC) with a 'foods with nutrient function claims' (FNFC) system and newly established FOSHU was introduced. In addition, the Govt. changed the existing FOSHU, FNFC and other systems in 2005. Such changes include the new Subsystems of FOSHU such as

- ✦ Standardized FOSHU
- ✦ Qualified FOSHU
- ✦ Disease risk reduction claims for FOSHU<sup>(8)</sup>

### CATEGORIES OF NUTRACEUTICALS<sup>(9)</sup>

Nutraceuticals are non-specific biological therapies used to promote wellness, prevent malignant processes and control symptoms. They are categorized as follows

## 1. Based on chemical constituents

### (a) Nutrients <sup>(10)</sup>

Substances with established nutritional functions, such as vitamins, minerals, amino acids and fatty acids. Common nutrients and their associated health benefits shown in Table 1.

### (b) Herbals <sup>(11)</sup>

Herbs or botanical products as concentrates and extracts. Common herbs and their therapeutic relevance are shown in Table 2.

### (c) Dietary Supplement

Dietary supplements are products administered through mouth that contain a dietary ingredient intended to add something to the foods you eat. Examples of dietary supplements are black cohosh for menopausal symptoms, ginkgo biloba for memory loss, and glucosamine/chondroitin for arthritis. They also serves specific functions such as sports nutrition, weight-loss supplements and meal replacements. Supplement ingredients may

contain vitamins, minerals, herbs or other botanicals, amino acids, enzymes, organ tissues, gland extracts, or other dietary substances. They are available in different dosage forms, including tablets, capsules, liquids, powders, extracts, and concentrates <sup>(12)</sup>. They could be categorized as shown in Table 3.

## 2. Traditional and Non- Traditional nutraceuticals

Wide variety of nutraceutical foods are available in the market which falls in the category of traditional foods and non traditional foods.

### (a) Traditional Nutraceuticals

Under the category of traditional Nutraceuticals comes food in which no change to the food are made; It is simply natural, whole foods with new information about their potential health qualities. There has been no change to the actual foods, other than the way the consumer perceives them.

**Table 1: List of nutrients and their relevance**

	Nutrients	Health benefit
1.	Vitamin A	Antioxidant, essential, for growth and development and in the treatment of certain skin disorders.
2.	Vitamin E	Antioxidant, helps form blood cells, muscles, lung and nerve tissue, boosts the immune system.
3.	Vitamin K	Essential for blood clotting.
4.	Vitamin C	Antioxidant, for healthy bones, gums, teeth and skin, in wound healing, prevent common cold and attenuate its symptoms.
5.	Vitamin B1	Helps to convert food in to energy, essential in neurologic functions.
6.	Vitamin B2	Helps in energy production and other chemical processes in the body, helps maintain healthy eyes, skin and nerve function.
7.	Vitamin B3	Helps to convert food in to energy and maintain proper brain function.
8.	Vitamin B6	Produce the genetic material of cells, formation of RBCs, maintenance of central nervous system and synthesize amino acids and metabolism of fats, protein and carbohydrates.
9.	Folic acid	Produce the genetic materials of cells, in pregnancy for preventing birth defects, RBCs formation, protects against heart disease.
10.	Calcium	Bones and teeth and maintaining bone strength important in nerve, muscle and glandular functions.
11.	Iron	Energy production, carry and transfer oxygen to tissues.
12.	Magnesium	Healthy nerve and muscle function and bone formation, may help prevent premenstrual syndrome (PMS).
13.	Phosphorous	Strong bones and teeth, helps in formation of genetic material, energy production and storage.
14.	Chromium	With insulin helps to convert carbohydrates and fats into energy.
15.	Cobalt	Essential component of vitamin B12, but ingested cobalt is metabolized <i>in vivo</i> to form the B12 coenzymes.
16.	Copper	Essential for hemoglobin and collagen production, healthy functioning of the heart, energy production, absorption of iron from digestive tract.
17.	Iodine	Essential for proper functioning of the thyroid.

**Table 2: Herbs used and their therapeutic relevance**

	Herbals (Botanical source)	Therapeutic activity
1.	Aloe vera gel ( <i>Aloe vera</i> L. N.L. Burm.)	Dilates capillaries, anti-inflammatory, emollient, wound healing properties.
2.	Chamomile ( <i>Matricaria recutita</i> L.)	Anti-inflammatory, spasmolytic, antimicrobial, wound Healing.
3.	Echinacea ( <i>Echinacea purpurea</i> L.)	Immunostimulant, treatment of cold and flu symptoms.
4.	Ephedra ( <i>Ephedra sinica</i> Stapf.)	Bronchodilator, vasoconstrictor, reduces bronchial Edema.
5.	Evening primrose oil ( <i>Oenothera biennis</i> L.)	Dietary supplement of linoleic acid, treatment of atopic eczema.
6.	Feverfew ( <i>Tanacetum parthenium</i> L.)	Treatment of headache, fever and menstrual problem, severity and duration of migraine headaches.
7.	Garlic ( <i>Allium sativum</i> L.)	Antibacterial, antifungal, antithrombotic, hypotensive anti-inflammatory.
8.	Ginger ( <i>Zingiber officinale</i> Rosc.)	Carminative, antiemetic, cholagogue, positive inotropic.
9.	Ginseng ( <i>Panax ginseng</i> )	Adaptogen.
10.	Ginkgo ( <i>Ginkgo biloba</i> L.)	Vasodilation, increased peripheral blood flow, Treatment of post thrombotic syndrome.
11.	Goldenseal ( <i>Hydrastis canadensis</i> L.)	Antimicrobial, astringent, antihemorrhagic, treatment of mucosal inflammation, dyspepsia, gastritis.
12.	Horehound ( <i>Marrubium vulgare</i> L.)	Expectorant, antitussive, cholaretic.
13.	Licorice ( <i>Glycyrrhiza glabra</i> L.)	Expectorant, secretolytic, treatment of peptic ulcer.
14.	Melissa ( <i>Melissa officinalis</i> L.)	Topical antibacterial and antiviral.
15.	Plantago seed ( <i>Plantago arenaria</i> Waldst)	Cathartic.
16.	St. John's wort ( <i>Hypericum perforatum</i> L.)	Anxiolytic, anti-inflammatory, antidepressant, monoamine oxidase inhibitor.
17.	Valerian ( <i>Valeriana officinalis</i> L.)	Spasmolytic, mild sedative, sleep aid.
18.	Willow bark ( <i>Salix alba</i> L.)	Anti-inflammatory, analgesic, antipyretic, astringent, treatment of rheumatic and arthritic.

**Table 3: Various categories of Dietary Supplements**

	Dietary supplements	Significance
1.	Ketogenic diets	Comprised of foods with high fat and low protein and carbohydrate content, have been reported to improve seizure control. However, these diets are widely acknowledged to be unpalatable <sup>(13)</sup> .
2.	Minimally refined grains	Cereals and grains fortified with calcium may reduce the incidence of diabetes <sup>(14)</sup> and prevents gastrointestinal cancers <sup>(15)</sup> .
3.	Phytoestrogens	Found in soya flour and linseeds and have been documented to enhance oestrogens levels when hormonal levels are low. This action may prevent against both hot flushes and breast cancer <sup>(16)</sup> .
4.	Several species of edible mushrooms	Tonnage, Lentinus, Pleurotus, Auricularia, Flammulina, Tremella, Hericium and Grifola have varying degrees of immunomodulatory, lipid lowering and antitumor without any significant toxicity.
5.	Glucosamine sulfate and chondroitin sulfate	They are effective and safer to alleviate symptoms of osteoarthritis <sup>(17)</sup> .
6.	Peptides/Hydrolysates	Found in casein and whey protein and have A.C.E.inhibitor activity <sup>(18)</sup> . Buckwheat proteins used as flour reduces cholesterol, hypertension; improve constipation and obesity by acting similar to dietary fibers and interrupting the in-vivo metabolism <sup>(19)</sup> .
7.	Dairy foods	Containing friendly or probiotic bacteria claimed to promote gut health. Bio yoghurts containing <i>Lactobacillus acidophilus</i> and Bifidobacteria lead the sector <sup>(20)</sup> .

Many fruits, vegetables, grains, fish, dairy and meat products contain several natural components that deliver benefits beyond basic nutrition, such as lycopene in tomatoes, omega-3 fatty acids in salmon or saponins in soy. Even tea and chocolate have been noted in some studies to contain health-benefiting attributes. Tomatoes and salmon are two types of food that researchers have found to contain benefits beyond basic nutrition - in this case, lycopene and omega-3 fatty acids, respectively.

## (2) Nontraditional Nutraceuticals

They are the outcome from agricultural breeding or added nutrients and/or ingredients such as orange juice fortified with calcium, cereals with added vitamins or minerals and flour with added folic acid are nontraditional nutraceutical. Agricultural scientists successfully have come up with the techniques to boost the nutritional content of certain crops. Research currently is being conducted to improve the nutritional quality of many other crops<sup>(21)</sup>.

## 3. Based on Diseases

TYPES OF DISEASES	NUTRACEUTICALS USED
<b>Cardiovascular diseases</b>	Anti-oxidants, Dietary fibres, Omega-3 poly unsaturated fatty acids, Vitamins, minerals for prevention and treatment of CVD. Polyphenol(in grape) prevent and control arterial diseases <sup>(22)</sup> Flavonoids (in onion, vegetables, grapes, red wine, apples, and cherries) block the ACE and strengthen the tiny capillaries that carry oxygen and essential nutrients to all cells <sup>(23)</sup> . Ethyl esters of n-3 fatty acids may be beneficial in diabetic patients <sup>(24)</sup> .
<b>Diabetes</b>	Docosahexaenoic acid modulates insulin resistance and is also vital for neurovisual development <sup>(25)</sup> . Lipoic acid, an antioxidant, for treatment of diabetic neuropathy <sup>(26)</sup> . Dietary fibers from psyllium have been used for glucose control in diabetic patients and to reduce lipid levels in hyperlipidemia <sup>(27)</sup> . Herbal stimulants, such as ephedrine, caffeine, ma huang-guarana, chitosan and green tea help in body weight loss <sup>(28)</sup> . Buckwheat seed proteins acting similar to natural fibers present in food <sup>(29)</sup> .
<b>Obesity</b>	5-hydroxytryptophan and green tea extract may promote weight loss, while the former decreases appetite, the later increases the energy expenditure <sup>(30)</sup> . A blend of glucomannan, chitosan, fenugreek, G sylvestre, and vitamin C in the dietary supplement significantly reduced body weight <sup>(31)</sup> . Conjugated linoleic acid (CLA), capsaicin, <i>Momordica Charantia</i> (MC) possesses potential anti obese properties <sup>(32)</sup> . Flavonoids which block the enzymes that produce estrogen reduce of estrogen-induced cancers <sup>(33)</sup> . To prevent prostate/breast cancer a broad range of phyto-pharmaceuticals with a claimed hormonal activity, called "phyto-estrogens" is recommended <sup>(34)</sup> . Soyfoods source of isoflavones, curcumin from curry and soya isoflavones possess cancer chemopreventive properties <sup>(35)</sup> .
<b>Cancer</b>	Lycopene concentrates in the skin, testes, adrenal and prostate where it protects against cancer <sup>(36)</sup> Saponins (found in peas, soybeans, some herbs, spinach, tomatoes, potatoes, alfalfa and clover) contain antitumor and anti-mutagenic activities <sup>(37)</sup> . Curcumin (diferuloylmethane) which is a polyphenol of turmeric possesses anticarcinogenic, antioxidative and anti-inflammatory properties <sup>(38)</sup> . Top of Form Beet roots, cucumber fruits, spinach leaves, and turmeric rhizomes, were reported to possess anti tumor activity <sup>(39)</sup> .
<b>Anti-inflammatory activities</b>	Gamma linolenic acid (found in green leafy vegetables, nuts, vegetable oils i.e.-evening primrose oil, blackcurrant seed oil, and hemp seed oil, and from spirulina, cyanobacteria) are used for treating problems with inflammation and auto-immune diseases <sup>(40)</sup> . Glucosamine and chondroitin sulfate are used against osteoarthritis and regulate gene expression and synthesis of NO and PGE2 (41). Cat's claw has 17 alkaloids, along with glycosides, tannins, flavonoids, sterol fractions, and other compounds and work as potent anti-inflammatory agent <sup>(42)</sup> .
<b>Allergy</b>	Quercet (found in Onions, red wine and green tea) reduce the inflammation that results from hay fever, bursitis, gout, arthritis, and asthma <sup>(43)</sup> .
<b>Alzheimer's disease</b>	$\beta$ -carotene, curcumin, lutein, lycopene, turmerin etc may exert positive effects on specific diseases by neutralizing the negative effects oxidative stress mitochondrial dysfunction, and various forms of neural degeneration <sup>(44)</sup>
<b>Parkinson's disease</b>	Vitamin E in food may be protective against Parkinson's disease <sup>(45)</sup> . Creatine modifies Parkinson's disease features as measured by a decline in the clinical signs <sup>(46)</sup> .

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### 3. Based on Diseases (*continued...*)

TYPES OF DISEASES	NUTRACEUTICALS USED
<b>Vision improving agents</b>	Lutein (found in mangoes, corn, sweet potatoes, carrots, squash, tomatoes and dark, leafy greens such as kale, collards and bok choy) also known as helenien is used for the treatment of visual disorders.  Zeaxanthin(found in corn, egg yolks and green vegetables and fruits, such as Broccoli, green beans, green peas, brussel sprouts, cabbage, kale, collard greens, Spinach, lettuce, kiwi and honeydew) used in traditional Chinese Medicine mainly for the treatment of Visual Disorders.
<b>Osteoarthritis</b>	Glucosamine (GLN) and chondroitin sulfate (CS) alleviate symptoms of O.A. <sup>(47)</sup> .

#### RESEARCH IN NUTRAGENOMIC

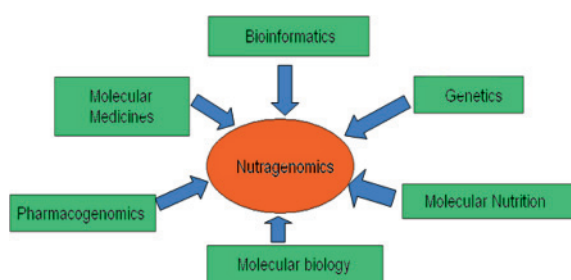
Genome science and technology is combined together to find new concept of food with a new function to prevent diseases, which is now termed as Nutraceuticals, further the genome technique called Nutrigenomics (nourishment genome science) was created. Nutrigenomics contains the three omics disciplines gene, protein, and metabolite profiling (transcriptomics, proteomics, and metabolomics) as applied to the field of nutrition and health. Nutrigenomics forms the scientific basis for developing nutrition adapted to the needs of consumer groups, to be healthy, at risk, or diseased. The term 'nutrigenetics' was first defined by RO Brennan in 1975 in his book Nutrigenetics. New Concepts for Relieving Hypoglycemia. Nutrigenomics is newly developed methodology combined with multiple genomic techniques and molecular biology technologies. Nutrigenomics is a technology involved in various academic fields as shown below, for scientific analysis of the relationship between food and food ingredients and health care and disease prevention<sup>(48)</sup>. A study on yeast showed that increasing the activity of a single gene, SIR2 could extend their life span. An analogous gene, SIRT1 was located in humans. Polyphenol such as Quercetin found in apples and tea, and Resveratrol (found in grape and red wine) were found to increase SRT1 activity in

a laboratory screening. Interestingly, Resveratrol was found to increase SRT1 activity 13-fold<sup>(49)</sup>. In terms of chronic diseases, particularly relevant are the effects of dietary cholesterol and fatty acids on gene expression. Dietary cholesterol exerts a profound inhibitory effect on the transcription of the gene for  $\beta$ -hydroxy- $\beta$ -methyl-glutaryl (HMG)-CoA reductase.

#### NUTRACEUTICAL SCENARIO IN INDIA

The Indian nutraceutical industry has great prospects. Over the last decade a wide range of products have been available, giving an insight into the tremendous growth. On one hand a booming economy has resulted in overall increase in disposable income of population. Added to this unhealthy, eating habits coupled with sedentary lifestyle have led to increase incidence of diet and its related health issues. On the other hand, there is a growing awareness on the importance of nutrition and diet for long term good health. These have contributed to a favorable market conditions for Nutraceutical industry in India. India has a lot of advantages like qualified human resources, world class R & D facilities and varied raw material-aspects that give our country a leading edge. The Indian Nutritional market is estimated to be USD 1 Billion. While the global market is growing at a CAGR of 7%, the Indian market has been growing much faster at a CAGR of 18% for the last three years, driven by Functional food and beverages categories. However the latent market in India is two to four times the current market size and is between USD 2 to USD 4 billion with almost 148 million potential customers. In USD 1 billion market size functional food having 54% market share followed by 32% market share of Dietary supplement and 14% share of Functional beverages. The Indian nutraceutical market is dominated primarily by pharmaceuticals and FMCG companies with very few pure play nutraceutical companies. Some major

**Figure 2: Relation between Nutrigenomic and other branches of life sciences (50).**



companies Marketing Nutraceuticals in India are GlaxoSmithKline consumer healthcare, Dabur India, Cadila Health care, EID Parry's, Zandu Pharmaceuticals, Himalaya herbal Healthcare, Amway, Sami labs, Elder pharmaceuticals and Ranbaxy<sup>(51)</sup>.

## CONCLUSION

Many nutraceuticals, functional foods and naturally occurring compounds that have been investigated and reported in various studies revealed that these products are extremely active, have profound effect on cell metabolism and often have little adverse effect. It is natural that people's focus is shifting to a positive approach for prevention of diseases to stay healthy. Nutraceuticals is scientific area generated all over the world. In many cases nutraceuticals offer an advantage over the synthetic drugs under development by the pharmaceuticals industry. It is novel pharmacological activity that are become interesting in their possible clinical use and thus helping in prevention and therapeutic in several diseases. Most of the pharmaceuticals companies often lack motivation to pursue these difficulties in obtaining the patents. It is hope that government agencies and research centers will give support for further research in nutraceuticals.

## CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest.

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